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TO STUDY THE CORRELATION OF URINARY URIC ACID AND CREATININE RATIO IN BIRTH ASPHYXIA

Pediatrics

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ABSTRACT

Introduction: Perinatal asphyxia is one of the leading causes of perinatal morbidity and mortality. Feasible and early biochemical markers to diagnose and predict the neurologic outcome is a great need of time as APGAR score alone is influenced by various factors. The present study was performed to determine the urinary uric acid to creatinine ratio in perinatal asphyxia and its correlation with APGAR score and compare urinary uric acid to creatinine ratio with Sarnat and Sarnat staging. **Materials and Methods:** This study was carried out on 100 term neonates with an equal number of cases and control 50 each, control group being the neonates with Apgar score ≥ 7 at 1 minute of life and cases being the neonates who suffered from perinatal asphyxia with Apgar < 7 at 1 minute of life. The spot urine sample was collected within 24 hours of birth and their uric acid and creatinine levels were measured and the ratio calculated. Asphyxiated neonates were classified according to Sarnat and Sarnat staging. We Compare UA/Cr ratio with Apgar score and HIE staging using Sarnat and Sarnat staging.**Results:** On comparison of UUA/Cr among cases and controls we found that ratio was significantly higher in asphyxiated neonates as compared to non asphyxiate neonates. (Control vs. Cases Group: 2.4 ± 1 vs. 3.6 ± 1.5; p –value < 0.0001). On comparison of UUA/Cr among cases with Sarnat and Sarnat staging of HIE, there is a significant difference observed in mean UA/Cr ratio across Sarnat and Sarnat staging of HIE (F – Value = 68.760; p – value = 0.0001). **Conclusion:** Urinary uric acid and creatinine ratio can be used as markers for perinatal asphyxia for screening in centers where other markers for assessing perinatal asphyxia are not available. Urinary uric acid and creatinine ratio is a non-invasive, cheap and easily available marker for assessing the severity perinatal asphyxia.

KEYWORDS

Birth asphyxia, Sarnat and Sarnat staging, Thompson score, Urinary Uric acid and creatinine ratio.

INTRODUCTION:

World Health Organisation (WHO) defines Perinatal asphyxia as "Failure to initiate or sustain breathing at birth."(1) Perinatal asphyxia is responsible for 9% (8 lakhs) of total under 5 mortality in the world accounting for the third most common cause of neonatal deaths following prematurity and bacterial infection.(2) In India, the neonatal mortality rate is 29 per 1000 live births and out of it, perinatal asphyxia accounts for 20% of 4 million newborn deaths.(3) The diagnosis of asphyxia is difficult if events at the time of labour are not available. Hypoxic-ischemic encephalopathy (HIE) refers to the central nervous system (CNS) dysfunction associated with perinatal asphyxia. HIE is the main concern in asphyxiated newborns because it leads to serious long term neuromotor sequel among survivors. Various biomarkers for diagnosing asphyxia and as prognostic marker such as Interleukin-6 (IL-6) in CSF, Neuron Specific Enolase (NSE) levels in CSF, Protein S-100b levels in serum, cord blood are being studied. But all the above biomarkers are expensive, time-taking and usually not available in all the labs/centers. Due to the lack of adequate oxygen supply during asphyxia, the formation of adenosine triphosphate (ATP) is impaired and this leads to an accumulation of adenosine diphosphate (ADP) and adenosine monophosphate (AMP), which are then catabolized to adenosine, inosine, and hypoxanthine. In cases of continuing tissue hypoxia, hypoxanthine is oxidized to xanthine and uric acid in the presence of xanthine oxidase; this leads to an increase in the urinary excretion of uric acid. In the reoxygenation period, radicals are produced parallel to uric acid formation, which may be linked to the severity of perinatal asphyxia. (4)

MATERIAL AND METHOD:

This study was carried out on 100 term neonates with an equal number of cases and control 50 each, cases being the neonates who suffered from perinatal asphyxia with Apgar < 7 at 1 minute of life and control group being the neonates with Apgar score ≥ 7 at 1 minute of life. The study was done in a neonatal unit of a tertiary care hospital in a rural setting of North Haryana. Detailed history of mother, perinatal and postnatal events were recorded on structured proforma. Asphyxiated neonates were classified according to Sarnat and Sarnat staging. Urine was collected using a pediatric urobag within 24 hours of birth. Urine was analyzed for uric acid and creatine levels by EBRA EM 360 fully automatic analyzer by applying the uricase method and Jaffe's reaction respectively and the ratio of uric acid and creatinine were calculated. Independent Student t-test was used for testing of mean value between independent groups whereas paired t-test was used for testing of the paired mean. One-way ANOVA was used for testing of mean between more than two independent groups. Crosstables were generated and the Chi-square test was used for testing of associations. Data analysis was done using SPSS software, version 24.0. We Compare UA/Cr ratio with Apgar score and HIE staging using Sarnat and Sarnat staging.

RESULTS:

In our study among 50 asphyxiated neonates,31 (62%) were in the Sarnat and Sarnat stage –I followed by 13 (26%) neonates in stage – II and 6 (12%) neonates in stage – III. On comparison, UA/Cr ratio was significantly higher in stage III (6.7±1.3) as compared tostage I (2.8±0.7; p-value = 0.0001) and significantly different from stage III (4.3±0.7; p-value = 0.0001). UA/Cr ratio was significantly higher in Stage II as compared to stage I (Moderate vs. Mild Grades: 4.3±0.7 vs. 2.8±0.7; p-value = 0.0001). It shows a significant difference in mean UA/Cr ratio across Sarnat and Sarnat staging of HIE (F – Value = 68.760; p-value = 0.0001). On comparison between cases and controls mean urinary UA/Cr ratio is significantly higher in the case group as compared to the control group. (Control vs. Cases Group: 2.4 ± 1 vs. 3.6 ± 1.5; p-value < 0.0001). On comparison between UA/Cr ratio and APGAR score at 1 and 5 minutes among cases significant correlation was observed between UA/Cr ratio and APGAR score at 1 (r =-0.427; p = 0.002) and 5 minutes (r =-0.456; p = 0.001) in the case group.

DISCUSSION:

In our study, we observed that there was a significant difference observed in the mean UA/Cr ratio across Sarnat and Sarnat staging of HIE (F – Value = 68.760; p-value = 0.0001).UA/Cr ratio was significantly higher in stage 3 (6.7 ± 1.3) as compared to stage 1 (2.8 ± 0.7; p – value = 0.0001) and significantly different from stage 2 (4.3 ± 0.7; p – value = 0.0001). UA/Cr ratio was significantly higher in stage 2 as compared to stage 1 (Stage 2 vs. Stage 1: 4.3±0.7 vs. 2.8 ± 0.7; p-value = 0.0001). In the study conducted by Mete Akisu et al (55) had mean UUA/Cr values in HIE 1, 2, 3 as 1.43 ± 0.29, 2.13 ± 0.36, 3.15 ± 0.81 respectively with p value < 0.01 which was statistically significant.(5).

On comparison between cases and controls mean urinary UA/Cr ratio is significantly higher in the case group as compared to the control group. (Control vs. Cases Group: 2.4 ± 1 vs. 3.6 ± 1.5; p-value < 0.0001). In the study conducted by Palb Basu et al UA/Cr ratio is higher among asphyxiated neonates than in non-asphyxiated neonates (3.1 ± 1.3 vs. 0.96 ± 0.54; p < 0.001). In our study mean values of controls are higher than the above study.(6)

A significant negative linear correlation between UA/Cr ratio and Apgar score at 1 (r = -0.427; p = 0.002) and 5 minutes (r =-0.456; p = 0.001) among asphyxiated neonates, which is similar to study conducted by **Pallab Basu et al** they also observed significant negative linear correlation between UUA/Cr and Apgar score. (r= -0.298, p = 0.103). (6).

CONCLUSION

- Urinary uric acid and creatinine ratio can be used as markers for perinatal asphyxia for screening in center where other markers for assessing perinatal asphyxia are not available.
- Urinary uric acid and creatinine ratio is a non-invasive, cheap and easily available marker for assessing the severity of perinatal asphyxia.

Limitations

- It is a single-center study with a small sample size, so the result could not be generalized to the whole population.
- Many birth asphyxia patients do not pass urine within 24 h of life.
- UUA/Cr ratio with other biochemical markers was not correlated, which could be more feasible and easily available.

Table 1: Mean value of urinary uric acid and creatinine ratio between cases and controls.

	Control Group	Cases Group	Std. Error Difference	95% CI of the Difference		t-value	p-value
				Lower	Upper		
UA/Cr	2.4±1	3.6±1.5	-1.3±0.3	-1.76	-0.75	-4.942	< 0.0001**

Table 2: Correlation between Study parameters and Apgar Score at 1 and 5 minutes.

	APGAR at 1 minute		APGAR at 5 minutes	
	Control Group	Cases Group	Control Group	Cases Group
UA/Cr	r =-0.078; p = 0.591	r =-0.427; p = 0.002*	r =0.056; p = 0.697	r =-0.456; p = 0.001*

Table 3: Comparison of mean value of urinary UA/Cr ratio between Sarnat and Sarnat staging of among cases.

Sarnat and Sarnat staging of HIE	UA/Cr		95% CI of the Difference		p-value
	Mean ± SD	Mean ± SE of Difference	Lower	Upper	
Stage 1	2.8±0.7	-1.5±0.3	-2.08	-.84	< 0.0001**
Stage 2	4.3±0.7				
Stage 1	2.8±0.7	-3.9±0.3	-4.71	-3.04	< 0.0001**
Stage 3	6.7±1.3				
Stage 2	4.3±0.7	-2.4±0.4	-3.33	-1.49	< 0.0001**
Stage 3	6.7±1.3				

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